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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF: Wong *et al.*	EXAMINER: K. Padmanabhan
SERIAL NO.: 09/517,597	ART UNIT: 1641
FILED: March 2, 2000	
FOR: **BIOSENSOR DEVICE AND METHOD**	

Response

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Reconsideration of the rejections set forth in the Office action dated January 13, 2003 is respectfully requested. Applicants petition the Commissioner for a 3-month extension of time; a separate petition accompanies this amendment. Claims 1-10 are currently under examination.

I. Rejection Under 35 U.S.C. §103(a)

Claims 1 - 10 were rejected under 35 U.S.C. §103(a) as being obvious over Lennox *et al.* (WO 97/41424). This rejection is respectfully traversed in view of the following remarks.

A. The Invention

The present invention relies on three key features, none of which is shown or suggested in the cited prior art:

1. producing a mobile "surrogate analyte" (the solution form of the coil-forming peptide) in an amount related to the amount of analyte, for reacting with the biosensor;

2. determining the presence or amount of analyte from a biosensor signal related to the amount of surrogate that binds to the biosensor; and

3. where the interaction of the surrogate with the biosensor is unrelated to the nature of the analyte.

These features provide several advantages over the biosensor methods and devices disclosed in the cited art. In particular,

1. the ability to detect both small- and large-molecule analytes in the same assay format. In the methods described in the cited art, biosensor signal is based on the perturbation of the biosensor surface produced by the binding of an (relatively large) anti-ligand analyte to a (relatively small) ligand molecule carried on the biosensor surface. All assay formats in the prior art devices require this configuration. In the present invention, the size of the analyte is not crucial, since the biosensor is responding to the interaction between two coil-forming peptides, not a ligand/anti-ligand interaction; and

2. the ability to design multi-analyte assays with a single type of biosensor. In the prior art, each biosensor requires an analyte-specific ligand carried on its surface. In the present invention, the biosensor has the same coil-forming peptide "receptor."

B. The Cited Art

Lennox (WO 97/41424) teaches a biosensor assay device for detecting a binding event between a ligand molecule attached to a biosensor surface and an anti-ligand molecule, whose binding to the biosensor-bound ligand perturbs the biosensor surface, producing a detectable biosensor signal. An array of biosensors is also disclosed. Nowhere does Lennox show or suggest the key features of the invention noted above, or the advantages achievable thereby.

As described on page 6, lines 18 - 24 of the reference, two peptide subunits are constructed and assembled in a manner that anchors a ligand on the biosensor surface. The first peptide subunit is attached directly to the surface, and the second subunit is attached to the ligand. Thus, in the cited reference no solution form of a coil-forming peptide occurs from reacting a liquid sample with an analyte-reaction reagent.

The next paragraph of the reference describes the two types of analyte-binding assays contemplated in the reference. The first is where the analyte is an antiligand molecule. In this case, the analyte can bind directly to the ligand molecule carried on the biosensor, to produce a biosensor signal. The second is where the analyte is a small-molecule (ligand). In this case, the assay further requires a ligand-binding agent that can bind both to the analyte and biosensor ligand. Thus, the prior art requires two different assay formats for ligand and anti-

ligand analytes, in contrast to the present invention.

C. Analysis

According to the MPEP § 2143, "to establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Third, the prior art reference (or references when combined) must teach or suggest all the claim limitations."

In the present case, the cited reference does not show or suggest the critical elements of the invention, as noted above. Even if these elements were disclosed in the cited reference, the prior art does not recognize the advantages of the invention, and thus provides no motivation for combining elements along the lines of the invention.

The Examiner states, "Although Lennox et al. does not teach the reaction of a sample with a reaction reagent to obtain a first coil-forming peptide, it would have been obvious to do so. Incorporation of the analyte-reaction reagent into the first coil forming peptide before reaction with the second coil forming peptide would have had the advantage of requiring fewer steps to carry out the process of determination of analyte presence."

However, the instant invention does not involve incorporation of the analyte-reaction reagent into the first coil forming peptide, and modifying Lennox according to the Examiner's suggestion would fail to produce the method of the invention, or any method capable of detecting an analyte present in the liquid sample. Lennox's invention, as described above, operates in a fundamentally different way than the present invention. If the analyte reaction reagent was incorporated into the first coil-forming peptide before reaction with the second coil forming peptide, it is not clear how Lennox's invention would be used to determine the presence of analyte, or which steps should be left out of Lennox's process to achieve the claimed invention. Claim 1 of the instant invention requires that the analyte is present in the liquid sample. If Lennox was modified according to the Examiner's suggestion by incorporating the analyte reaction reagent into the first coil-forming peptide before binding to the second coil-forming peptide, and the analyte was present in the liquid sample as is required in claim 1, the biosensor would not have the ability to determine the presence of analyte. Binding of the analyte to the first coil-forming peptide/reaction reagent conjugate would not have any effect on

the binding of the conjugate to the second coil-forming peptide. The conjugate would be free to bind to the second coil-forming peptide in the absence or presence of analyte, thus defeating the purpose of the invention. With such a modification, there would be no signal generated which could be correlated to the presence of the analyte in the sample as is required in claim 1 of the instant invention.

The Examiner also states, "In addition, whether the analyte-reaction reagent is contacted with the first coil-forming peptide before contact with the second peptide, or whether it was contacted to the complex after heterodimer formation, the end result would have been the same, and one or ordinary skill in the art would have recognized that either protocol could have been used with a reasonable expectation of success. In either mechanism, a receptor on the heterodimer complex would bind to analyte to allow for analyte determination."

The analyte-reaction reagent in the instant invention is not required to contact the first coil-forming peptide either before or after heterodimer formation. The analyte-reaction reagent reacts with the liquid sample. The first coil-forming peptide generated by that reaction contacts the second coil-forming peptide on the biosensor surface. And no receptor on the heterodimer complex binds to the analyte to allow for analyte determination.

For the reasons presented above, claim 1 cannot be considered obvious over the cited art or any other art known to the applicants. The remaining pending claims, which depend from claim 1, define over the prior art for the same reasons that claim 1 does.

Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §103.

II. Conclusion

In view of the above remarks, the applicants submit that the pending claims are in condition for allowance. A Notice of Allowance is, therefore, respectfully requested.

If in the opinion of the Examiner a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 838-4405.

Respectfully submitted,

Date: 7-14-03

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